Enhanced CLIP Uncovers IMP Protein-RNA Targets in Human Pluripotent Stem Cells Important for Cell Adhesion and Survival.

Journal: Cell Rep

Publication Year: 2016

Authors: Anne E Conway, Eric L Van Nostrand, Gabriel A Pratt, Stefan Aigner, Melissa L Wilbert, Balaji Sundararaman, Peter Freese, Nicole J Lambert, Shashank Sathe, Tiffany Y Liang, Anthony Essex, Severine Landais, Christopher B Burge, D Leanne Jones, Gene W Yeo

PubMed link: 27068461

Funding Grants: RNA Binding Protein-mediated Post-transcriptional Networks Regulating HPSC Pluripotency, Neural and general splicing factors control self-renewal, neural survival and differentiation, Molecules to Correct Aberrant RNA Signature in Human Diseased Neurons, Stem cell models to analyze the role of mutated C9ORF72 in neurodegeneration

Public Summary:
Human pluripotent stem cells (hPSCs) require precise control of post-transcriptional RNA networks to maintain proliferation and survival. Using enhanced UV crosslinking and immunoprecipitation (eCLIP), we identify RNA targets of the IMP/IGF2BP family of RNA-binding proteins in hPSCs. At the broad region and binding site levels, IMP1 and IMP2 show reproducible binding to a large and overlapping set of 3' UTR-enriched targets. RNA Bind-N-seq applied to recombinant full-length IMP1 and IMP2 reveals CA-rich motifs that are enriched in eCLIP-defined binding sites. We observe that IMP1 loss in hPSCs recapitulates IMP1 phenotypes, including a reduction in cell adhesion and increase in cell death. For cell adhesion, we find IMP1 maintains levels of integrin mRNA specifically regulating RNA stability of ITGB5 in hPSCs. Additionally, we show that IMP1 can be linked to hPSC survival via direct target BCL2. Thus, transcriptome-wide binding profiles identify hPSC targets modulating well-characterized IMP1 roles.

Scientific Abstract:
Human pluripotent stem cells (hPSCs) require precise control of post-transcriptional RNA networks to maintain proliferation and survival. Using enhanced UV crosslinking and immunoprecipitation (eCLIP), we identify RNA targets of the IMP/IGF2BP family of RNA-binding proteins in hPSCs. At the broad region and binding site levels, IMP1 and IMP2 show reproducible binding to a large and overlapping set of 3' UTR-enriched targets. RNA Bind-N-seq applied to recombinant full-length IMP1 and IMP2 reveals CA-rich motifs that are enriched in eCLIP-defined binding sites. We observe that IMP1 loss in hPSCs recapitulates IMP1 phenotypes, including a reduction in cell adhesion and increase in cell death. For cell adhesion, we find IMP1 maintains levels of integrin mRNA specifically regulating RNA stability of ITGB5 in hPSCs. Additionally, we show that IMP1 can be linked to hPSC survival via direct target BCL2. Thus, transcriptome-wide binding profiles identify hPSC targets modulating well-characterized IMP1 roles.